Guillain-Barré Syndrome in Military Populations

Navy Environmental Health Center
23 March 2006
Paul D. Rockswold, MD, MPH
CDR, MC, USN (UMO)

Notice

- Disclaimer
  - The views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.
- Research Ethics Statement
  - I declare no conflicts of interest or financial interests in any product or service mentioned in this article, including grants, employment, stock holdings, gifts, or honoraria.
  - All study results and data in this presentation met required research subject protection regulations.

Recruits

- Navy at Great Lakes, IL
  - Increasing annual trend (0, 0, 2, 4, 6)
  - Increased use of EMR
- Marine Corps at Parris Island, SC
  - 3 cases over several years
  - 2 cases in January 2005
- ± Army and Air Force

Guillain-Barré Syndrome (GBS)

Objectives

- List current concepts from the literature
- Describe results of Navy studies on GBS
- List future steps

The Syndrome

- Acute infective polyneuritis (autoimmune)
- Symmetric ascending paralysis
- Possible ventilator therapy

Incidence

- Rare (cases per 100,000 [person-years])*
  - 0.4 - 1.5 in temperate climates
  - 0.8 in those under 18 years
  - 3.25 in those over 60 years
- Reported rates from various sources
  - 0.4 - 4 cases per 100,000 person-years
- Type and incidence are different in different parts of the world

*__Cohen & Powderly: Infectious Diseases, 2nd ed.__, Copyright © 2004 Elsevier

Conditions Associated with GBS

- Non-specific respiratory tract symptoms (50%)
- Campylobacter jejuni (26-40%)
- Mycoplasma pneumoniae
- Cytomegalovirus
- Epstein-Barr virus
- HIV-1
- Japanese encephalitis virus
- Hodgkin's disease
- Lymphoma
- Systemic lupus erythematosus
- Surgery
- Parturition
- Vaccines (<5%)
  - Vaccinia
  - Rabies
  - Influenza A/New Jersey/76
  - Oral poliovirus in Finland

Other Notes

- Associations
  - Swine flu vaccine 1968 (OR = 6)
  - West Nile Virus
- Potential Biases
  - Estimates of rare conditions
  - Chart abstraction vs. electronic data
- Poisson vs. Normal statistical methods

Questions

- Do military rates differ from literature?
- Are there sub-populations in the military with higher rates?
- Do rates differ between military services?

Guillain-Barré Syndrome (GBS) Objectives

1. List current concepts from the literature
2. Describe results of Navy studies on GBS
3. List future steps

Studies

1. Case rate estimate
2. VAERS comparisons
3. M2 Inpatient Incident Cases
    1. Feb 2005
    2. April 2005
4. Line listing comparison
5. Proportional Hazards Regression
6. Multiple Vaccinations

Poisson Regression

Year	Count	At Risk	95% Confidence Interval on Observed		
			95% LCL	Rate / 100k	95% UCL
2001	2	51.160	0.47	3.91	14.12
2002	4	43.777	2.49	9.14	23.39
2003	6	40.418	5.45	14.84	32.31

Year	1-sided p-values against reference rates					
Ref*	0.4	0.8	1	2	4	8
2001	**0.018**	0.064	0.094	0.273	0.606	0.915
2002	**<0.0001**	**0.0005**	**0.001**	**0.012**	0.101	0.464
2003	**<0.0001**	**<0.0001**	**<0.0001**	**0.0002**	**0.006**	0.109

Bolded values => statistically significant

*multiple p-values are calculated using typical rates reported in the literature.

Results derived from data from Zajdowicz, MJ, Feb 2004.

“Statistically Significant” What are the causes?

- True difference
  - Apply existing scientific knowledge
- Artifact due to
  - Random error
    - Large sample size
    - Multiple well designed studies
  - Study bias
    - Identify and eliminate
  - Confounding
    - Identify and eliminate

Review: VAERS 1990 – 2004*

- 14 year period
- Considered case if in any of 20 fields
- 171,506 records
- 149,542 (87.2%) with known onset date
  - Records with missing dates are similar to those with dates

*Derived from Sheets, J S 2004 Powerpoint

VAERS Known onset date*

n Row %	GBS	Non-GBS	
Military	37 0.52%	7,013 99.48%	7,050 100%
Non-Military	769 0.54%	141,723 99.46%	142,492 100%
	806	148,736	149,542

- OR = 1.02 (0.71 – 1.42)
- χ^2 = 0.01 (p = 0.90 Fisher's Exact)
- No difference in reporting proportions

*Derived from Sheets, J S 2004 Powerpoint

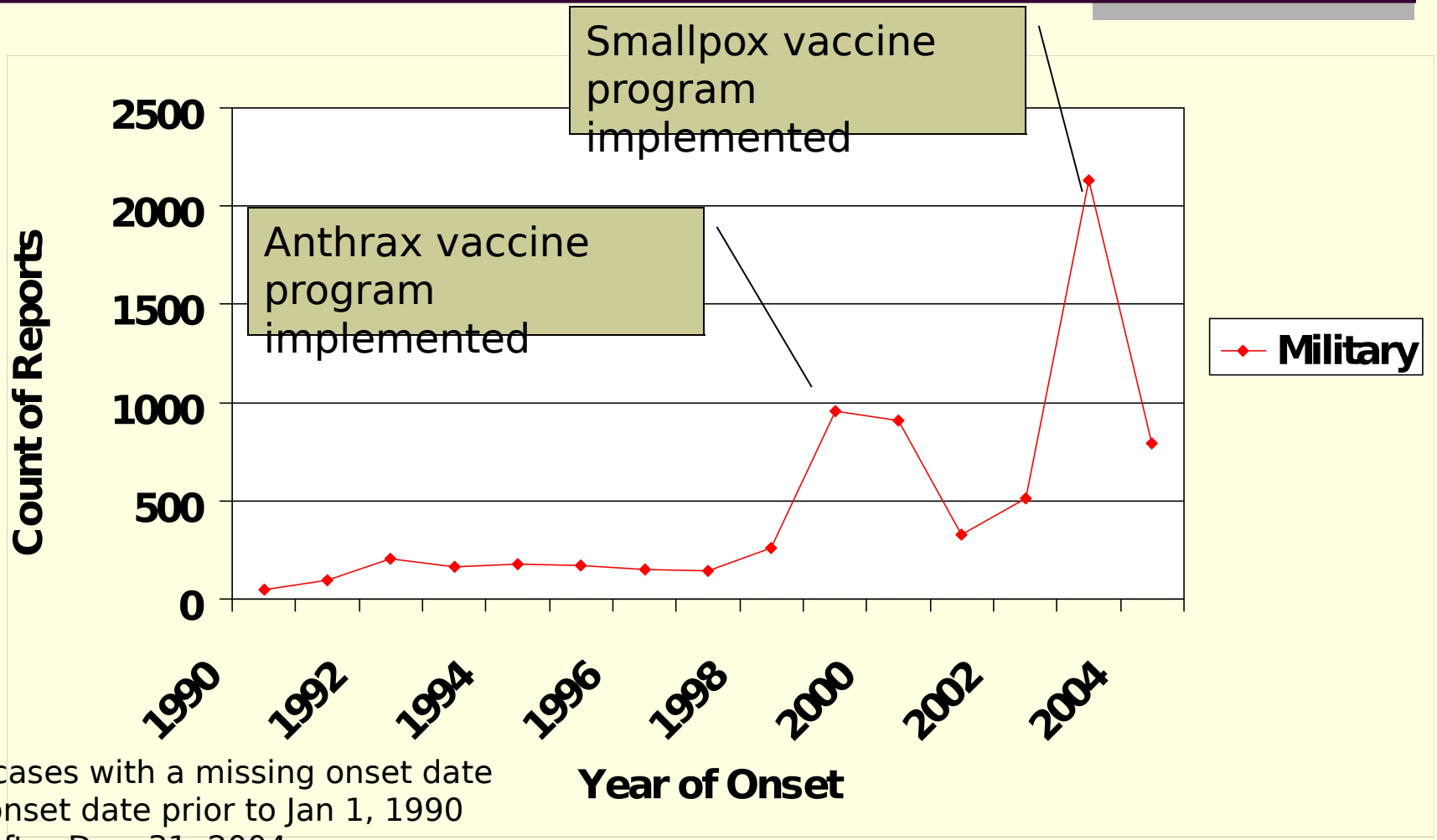
VAERS Known onset date* 18-24 year old sub-analysis

n Row %	GBS	Non-GBS	
Military	9 0.60%	1,496 99.40%	1,505 100%
Non-Military	25 0.45%	5,544 99.55%	5,569 100%
	34	7,040	7,074

- OR 1.33 (0.55 – 2.96)
- $\chi^2 = 0.55$ (p = 0.45, Fisher's Exact)
- No difference in reporting proportions

*Derived from Sheets, J S 2004 Powerpoint

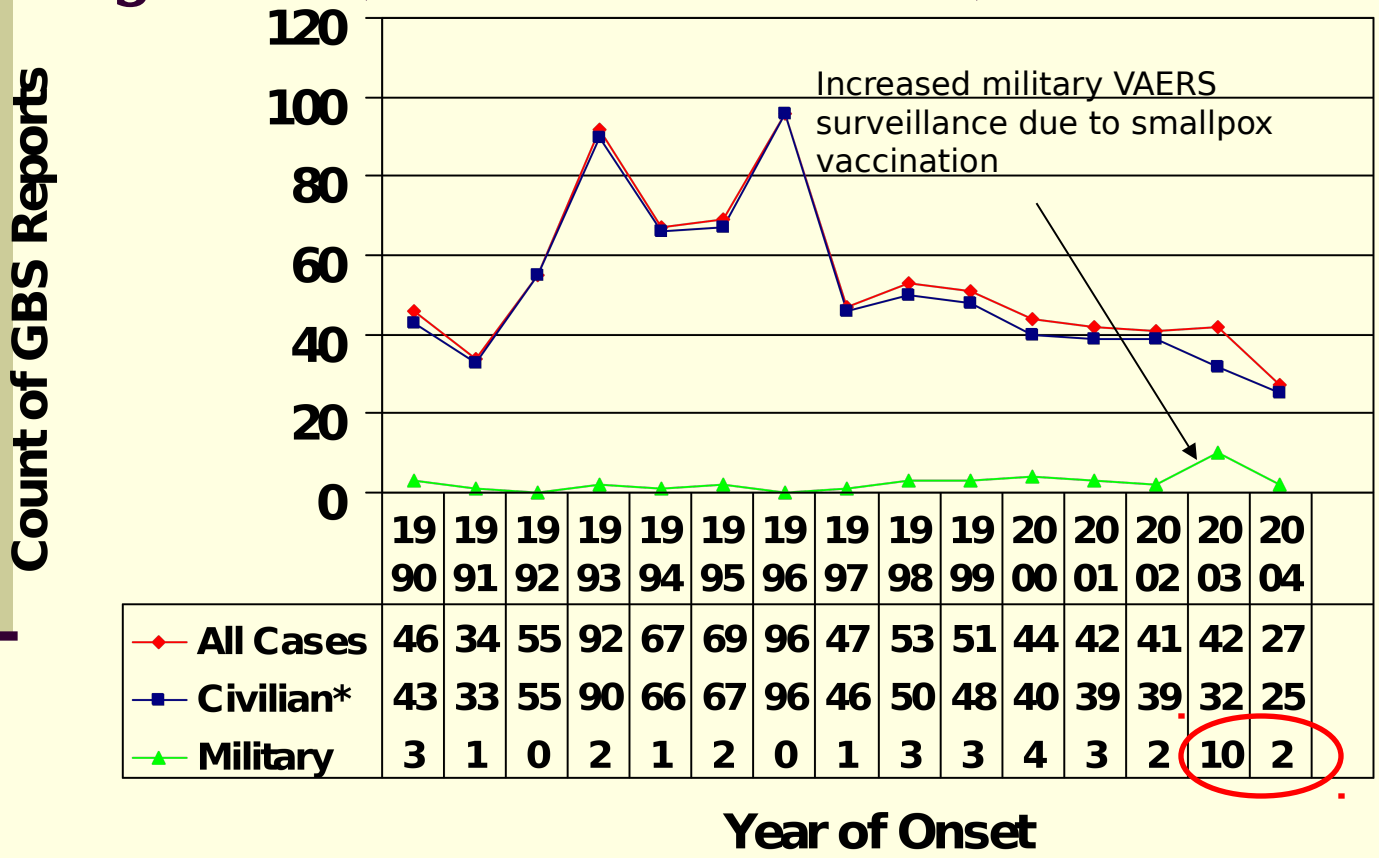
All VAERS Reports-Military Jan 1,1990-Dec 31, 2004



All cases with a missing onset date or onset date prior to Jan 1, 1990 or after Dec. 31, 2004 were deleted.

*Derived from Sheets, J S 2004 Powerpoint

GBS VAERS Reports by Onset Date
Jan 1,1990-Dec 31, 2004



	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
All Cases	46	34	55	92	67	69	96	47	53	51	44	42	41	42	27
Civilian*	43	33	55	90	66	67	96	46	50	48	40	39	39	32	25
Military	3	1	0	2	1	2	0	1	3	3	4	3	2	10	2

*Cases with a missing value for either/both the Vaccine Administered by or the
Vaccine Funded by categories are included in the civilian category
All Cases with a missing onset date or onset date prior to 1990 were

VAERS Summary

- No difference in proportionate reporting
- Counts only show difference in 2004
  - Indicator for recruits not available
- Low number of VAERS vs. GBS incidence
  - Poor reporting
  - Clinician attitude that GBS is not vaccine associated.

Studies

1. Case rate estimate
2. VAERS comparisons
3. M2 Inpatient Incident Cases
    1. Feb 2005
    2. April 2005
4. Line listing comparison
5. Proportional Hazards Regression
6. Multiple Vaccinations

M2 Inpatient

- Period
- Sources
- Numerators
- Populations

M2 Studies (Navy and Marines)

Study Performed	Interval Start	Interval End	Included ICDs (Numerator)	Population Source
Feb 2005	JAN 1999	DEC 2004	357.0	DMED
April 2005	JAN 1999	JAN 2005	357.0 & 357.9	M2 Enrollment

M2 Preliminary Finding

- 6y1m period
- 158 first diagnoses recorded (Outpatient)
  - Concern that prevalent cases may be considered incident
  - Denominator data not available yet
  - Rates cannot be calculated until denominators available

Studies

1. Case rate estimate
2. VAERS comparisons
3. M2 Inpatient Incident Cases
    1. Feb 2005
    2. April 2005
4. Line listing comparison
5. Proportional Hazards Regression
6. Multiple Vaccinations

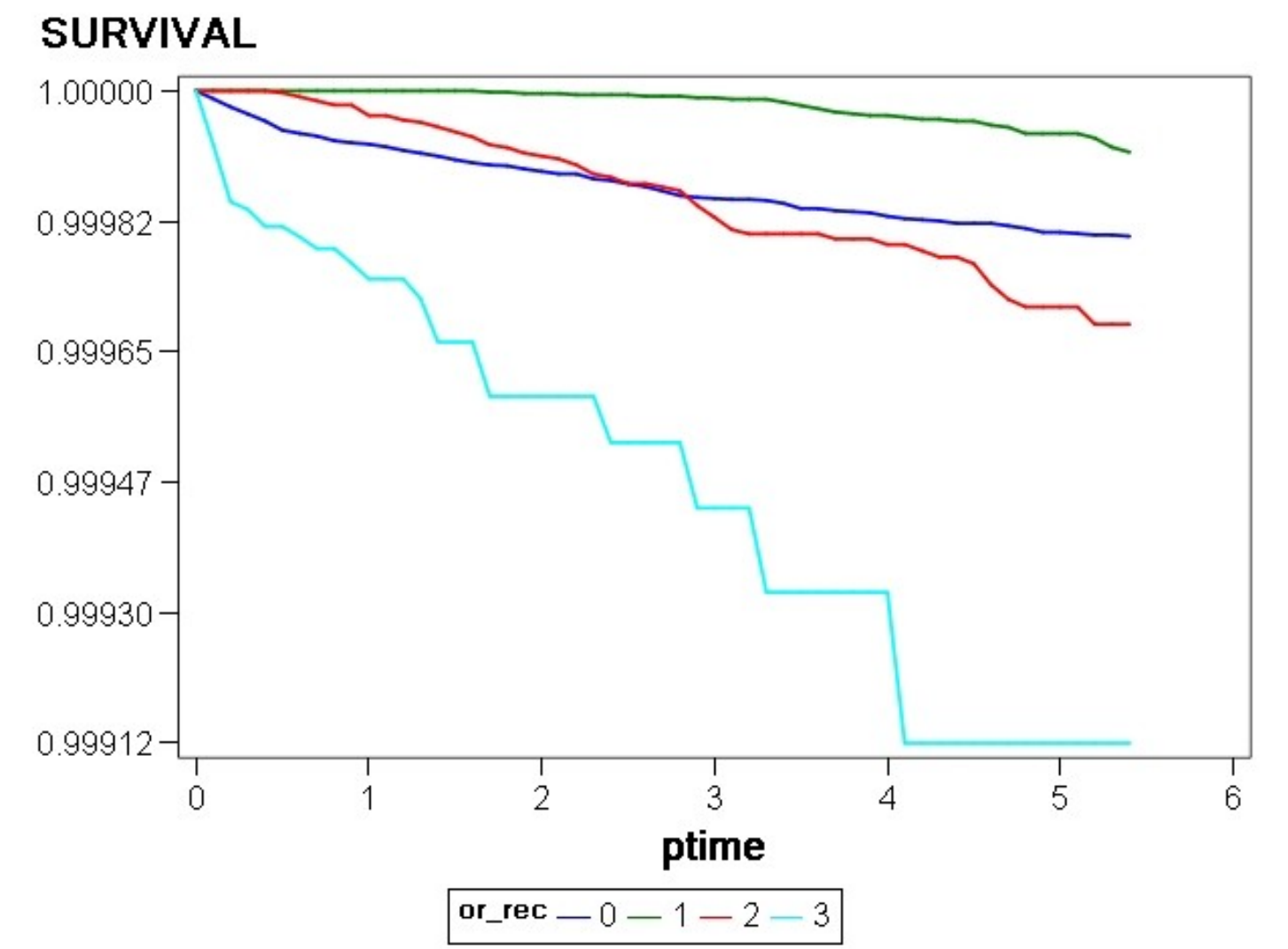
NHRC Study (Preliminary)

- Cox Proportional Hazards
- All AD
  - Period 1OCT1998 – 31MAR2004
  - 2,305,513 AD
  - 123 Excluded for prior diagnosis
  - 8,592,307 person-years
  - 314 incident cases (Crude 3.7/100k person-years)

NHRC Study Method

- Identify “exposures”
  - Respiratory diagnoses
  - GI diagnoses
  - Other diagnoses
- Adjust for significant variables
  - e.g. age, sex, marital status, education
- Compare hazards between “exposure” groups.

Disease Free Proportion by Respiratory Disease "Exposure" (Preliminary)



Studies

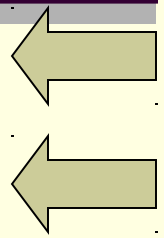
1. Case rate estimate
2. VAERS comparisons
3. M2 Inpatient Incident Cases
    1. Feb 2005
    2. April 2005
4. Line listing comparison
5. Proportional Hazards Regression
6. Multiple Vaccinations

Guillain-Barré Syndrome (GBS) Objectives

- List current concepts from the literature
- Describe results of Navy studies on GBS
- List future steps

Epidemiologic Principles

- Care for those that are affected
- Implement effective prevention measures



- Epidemiology study steps
  - Determine denominators and rates for M2 study
  - Compare line listings to administrative data
- Advance knowledge where possible with well designed studies
  - Finish NHRC Cox Regression study
  - Multiple vaccine study by NHRC

Preventive Measures

- Expected benefit
  - Decrease respiratory infections
  - Decrease GI illness
  - Resume adenovirus vaccinations
- Uncertain benefit
  - Space immunizations out

Summary

- List current concepts from the literature
- Describe results of Navy studies on GBS
- List future steps